1-25-93

DP BARCODE : D172585

PC Code No.: 128992

Date Out of EFGWB: JAN 25 1993

TO: Phillip Hutton/Mike Mendelsohn
Product Manager #18
Registration Division (H7505C)

FROM: Akiva D. Abramovitch, Ph.D., Section Head
Environmental Chemistry Review Section #3
Environmental Fate and Ground Water Branch, EFED (H7507C)

THRU: Henry M. Jacoby, Chief
Environmental Fate and Ground Water Branch/EFED (H7507C)

Attached, please find the EFGWB review of:

Reg./File #: 001812-00327

Common Name: Sulfluramid

Chemical Name: N-Ethylperfluorooctanesulfonamide

Type product: Insect bait

Product Name: GX-071, Technical

Company Name: Griffin Corporation

Purpose: Review of Hydrolysis and Adsorption/Desorption (Batch equilibrium) Studies

Action Code: 400 EFGWB #: 92-0352 Total Reviewing Time: 3.0 days

EFGWB Guideline/MRID Summary Table: The review in this package contains:

161-1 42123001	162-1	164-1	165-1	166-1
161-2	162-2	164-2	165-2	166-2
161-3	162-3	164-3	165-3	166-3
161-4	162-4	164-4	165-4	167-2
201-1	163-1 42154701	164-5	165-5	167-3
202-1	163-2/-3			

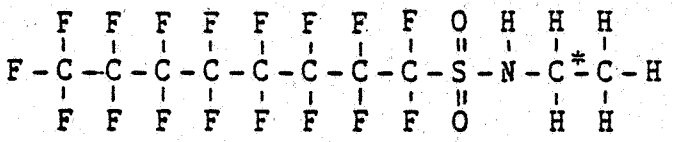
1. CHEMICAL

Common Name: Sulfluramid; Company Code "GX071"

Chemical Name: N-Ethylperfluoroctanesulfonamide

Chemical Abstracts Reg. #: 4151-50-2

Chemical Structure:



Physical/Chemical Properties (as reported):

Molecular weight: 527
Empirical formula: $C_8H_{17}SO_2N(H)CH_2CH_3$
Physical state: Solid
Color: White
Melting point range: 93.0 - 96.5 C
Boiling point: 110 C (at 2 mmHg)
Bulk density: 0.1485 g/mL (25 C)
Solubility (at 25 C):

Water	Nil
Hexane	1.4%
Methylene Chloride	1.86%
1-Octanol	7.09%
Methanol	83.3%

$LogP_{ow}$ = >6.05 (calc.); 3.10 (observed)
Vapor pressure at 25 C: 4.3 x 10^{-7} (units?)
Dissociation constant: 3.16 x 10^{10}

Mode of action: Preliminary data indicate that sulfluramid is an uncoupler of oxidative phosphorilation in isolated mitochondria.

2. TYPE OF ACTION:

Review of Hydrolysis (161-1) and Mobility in Soil, Unaged (163-1) studies.

3. STUDY IDENTIFICATION:

161-1, Hydrolysis
Spare, W.C. and Jensen, M.P. 1991. Hydrolysis of ^{14}C-GX071. Performed by Agrisearch, Inc., Frederick, MD. Laboratory Project ID #2514; Completed 3/20/91.
MRID #42123001

2

163-1 Mobility in Soil (Unaged)
Spare, W.C. 1991. Adsorption/Desorption of ^{14}C-GX071. Performed by Agrisearch, Inc., Frederick, MD. Laboratory Project ID #2515. Completed 1/16/91.
MRID #42154701

The studies were submitted by Griffin Corporation, Valdosta, GA.

4. REVIEWED BY:

Silvia C. Termes, Chemist
Review Section #3
OPP/EFED/EFGWB

Signature: _____
Date: January 21, 1993

5. APPROVED BY:

Akiva D. Abramovitch, Ph.D.
Section Head, Review Section #3
OPP/EFED/EFGWB

Signature: _____
Date: _____

6. CONCLUSIONS:

A. Administrative

a. The Hydrolysis study SATISFIES the 161-1 data requirement.

b. The Mobility in Soil study is acceptable and PARTIALLY SATISFIES the 163-1 data requirements. The study provides information on the mobility of parent sulfluramid (GX071), unaged, in four soils.

If significant degradation products are found in the photodegradation and/or aerobic soil metabolism studies, batch-equilibrium adsorption/desorption studies with each of the major degradates may be required. Therefore, data from these studies are necessary before determining if data on mobility of major degradates are necessary.

The only additional information that EFGWB is requesting at this time relates to the mineralogy of the soils used in the reviewed study as well as their origin.

B. Scientific

Data from the hydrolysis indicate that parent sulfluramid (GX071) is stable to hydrolysis in pH 5, 7, and 9 buffered solutions incubated in the dark at 25 C for 30 days (sterile conditions). Although no attempts were made to minimize/prevent adsorption onto the test equipment, data presented in the batch-equilibrium adsorption/desorption study showed that adsorption (considerable) occurs even when silanization and methylation of the test equipment was done prior to the study.

Data from the batch-equilibrium adsorption/desorption study showed that sulfluramid adsorbed strongly onto the four different soils (ranging in texture from sand to clay) and that once adsorbed, it does not desorbs back into the solution phase. This indicates that sulfluramid is expected to be immobile. The results are summarized below (see Table 1 in the Data Evaluation Record for soil characteristics). Note that the values of n deviate from 1 (i.e., adsorption deviates from linearity).

Series/Texture	Sharkey Clay	Sassafras Sand	Sequatchie Sandy Loam	Hesperia Loam
Source	Mississippi	Maryland	Maryland	California
n	0.783	0.831	0.664	0.667
K_{ads}	623	118	2296	1257
K_{oc}	22,436	22,383	205,466	267,130
%O.C (%O.M.)	2.8 (4.8)	0.53 (0.9)	1.1 (1.9)	0.47 (0.8)
pH	5.9	6.5	7.5	6.7

7. RECOMMENDATIONS:

Inform the registrant that the Hydrolysis data requirement is SATISFIED. The Mobility in Soil (unaged) study PARTIALLY SATISFIES the 163-1 requirement at this time.

The registrant should be made aware that batch-equilibrium adsorption/desorption studies with major degradates may be required if such degradates are identified in photodegradation and/or metabolism studies. If sulfluramid is shown to be stable towards photodegradation and biodegradation, then the the 163-1 data requirement may be satisfied with the unaged study alone.

The Branch would greatly appreciate if the registrant supplies the data on soils requested in the CONCLUSIONS section.

8. BACKGROUND:

Sulfluramid is currently registered for indoor uses as roach and ant traps (baits). The only data requirement for indoor uses is hydrolysis, which is now satisfied.

The registrant is currently seeking uses that involve outdoor applications that fall within the terrestrial non-food use pattern (see EUP request 001812-EUP-E; DP BARCODE 179984; EFGWB #92-1107).

For information on previous meetings between the registrant and EFGWB refer to EFGWB #90-0889; 10/16/90).

9. DISCUSSION OF INDIVIDUAL STUDIES: See corresponding DERs.

10. COMPLETION OF ONE-LINER: The One-Liner has been updated with the information provided by the two reviewed studies.

11. CBI APPENDIX: No CBI

DATA EVALUATION RECORD

STUDY 1

CHEM 128992 Sulfluramid §161-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42123001
Spare, W.C., and M.P. Jensen. 1991. Hydrolysis of ^{14}C-GX071. Agrisearch Project No. 2514. Unpublished study performed by Agrisearch Inc., Frederick, MD, and submitted by Griffin Corporation, Valdosta, GA.

DIRECT REVIEW TIME = 12

REVIEWED BY: D. Martinez TITLE: Staff Scientist

EDITED BY: K. Ferguson TITLE: Task Leader
W. Hurtt Staff Scientist

APPROVED BY: W. Spangler TITLE: Project Manager

ORG: Dynamac Corporation
Rockville, MD
TEL: 301-417-9800

APPROVED BY: S. Termes
TITLE: Chemist
ORG: EFGWB/EFED/OPP
TEL: 703-305-5243

SIGNATURE: Jan. 12, 1993

CONCLUSIONS:

This study may be used towards fulfilling the Hydrolysis (161-1) data requirement. Although considerable adsorption onto the test equipment (glassware and particularly, Teflon caps) occurred and no attempts to minimize adsorption were made, data from the batch-equilibrium adsorption/desorption studies (MRID #42154701) showed that silanization and methylation were not effective in preventing adsorption to the equipment.

The data presented indicate that GX071 is likely to be stable to hydrolysis at pHs 5, 7, 9. The nature of the material in the Teflon caps was not clearly established in spite of the many attempts made.

5

METHODOLOGY:

N-ethyl-labeled [1-^{14}C]sulfluramid (radiochemical purity 99.8%, specific activity 14.1 mCi/mMol, New England Nuclear) in methanol was added at 0.14 ppm to sterile aqueous buffer solutions that had been adjusted to pH 5 (0.01 M acetate), pH 7 (0.067 M phosphate), and pH 9 (0.025 M borate). Aliquots (15 mL) of the treated buffer solutions were transferred into sterile, foil-covered 22-mL glass vials, and the vials were sealed with Teflon-lined caps. The samples were incubated in the dark at 25 ± 1 C. Duplicate vials of each buffer solution were removed for analysis at 0, 1, 3, 7, 14, and 30 days posttreatment.

Following removal of the samples from the incubation chamber, toluene (2 mL) was added to the vials containing the treated solutions. The 0- and 1-day samples were vigorously shaken by hand for 30 seconds, then the toluene fraction was removed with a pipette and the aqueous fraction was decanted from the vial. The 7- through 30-day samples were partitioned twice with toluene, each time by shaking on a mechanical shaker for approximately 30 minutes. For the 3-day samples only, the samples were extracted once with toluene by hand shaking and once with mechanical shaking as previously described. Duplicate aliquots of the organic fraction from each partitioning were analyzed for total radioactivity using LSC (the two 30-day organic fractions were combined prior to LSC analysis); duplicate aliquots of the residual aqueous fraction were analyzed using LSC.

Additional aliquots of the toluene extracts were analyzed for sulfluramid by one-dimensional TLC on two sets of silica gel plates; one set of plates was developed in toluene:acetone (3:1, v:v), and the second set in chloroform:methanol:formic acid:water (75:25:8:2, v:v:v:v). Radioactive compounds were located and quantified using a linear scanner. An unlabeled sulfluramid reference standard, that was cochromatographed with the test solutions, was visualized using Erlich's reagent. In order to confirm the identity of sulfluramid, the aliquots of the 30-day posttreatment samples prior to partitioning, and aliquots of the toluene extracts from the 30-day sample, were analyzed by GC with electron capture detection.

Following decanting of the liquid fractions from the vials, the Teflon-cap liners were cut into small fragments and returned to their original vial. The glass vials were then filled with scintillation fluid, sealed with a new cap, and allowed to stand for 45 to 60 days. Aliquots of the scintillation fluids were then analyzed using LSC. Vials from the 3- through 14-day sampling intervals were heated for 6 hours at 90 C, and vials from the 30-day sampling were heated for 3 days at 60 C. The scintillation solutions were reanalyzed using LSC. Attempts to identify radioactivity in caps and vials were made using fractional distillation, direct GC analysis, and Sep-Pak and Florisil column chromatography; a description of these procedures was not

provided. The study authors stated that because of the presence of large amounts of fluors and emulsifiers in solution, it was not possible to separate significant amounts of radioactivity from the scintillation fluid.

DATA SUMMARY:

N-ethyl-labeled [1-^{14}C]sulfluramid (radiochemical purity 99.8%), at 0.14 ppm, appeared to be stable in sterile aqueous pH 5, 7, and 9 buffer solutions that were incubated in the dark at 25 ± 1 C for 30 days. [^{14}C]Sulfluramid comprised ≥95.9% of the radioactivity recovered from the buffer solutions at all sampling intervals; however, the concentration of [^{14}C]sulfluramid recovered from the buffer solutions decreased steadily during the experiment (Table VI). Immediately posttreatment, [^{14}C]sulfluramid comprised 96.9-110.8% of the applied in all three solutions. By 30 days posttreatment, [^{14}C]sulfluramid had decreased to 32.1-43.3% of the applied in the pH 5 solution, 23.1-41.6% in the pH 7 solution, and 47.9-60.2% in the pH 9 solutions. At 30 days posttreatment, the majority (maximums of 56.9-70.4%) of the radioactivity applied to the solutions had absorbed to the Teflon cap liners; these [^{14}C]residues were assumed to be sulfluramid (Tables III-V). During the study, the material balances ranged from 78.6% to 111.1% of the applied with no discernable pattern.

COMMENTS:

1. The majority of the radioactivity applied to the buffer solutions absorbed to the Teflon cap liners and was not in solution. Of the radioactivity applied to the pH 5, 7, and 9 buffer solutions, maximums of 56.9-70.4% were recovered from the Teflon cap liners. The study authors stated that there are similarities between the chemical structures of sulfluramid and Teflon, and that sulfluramid "literally dissolved into the perfluoroethylene matrix of the Teflon cap liners". Since the structures of Teflon and sulfluramid were known prior to the start of the experiment, the problem of absorption should have been anticipated and equipment should have been selected to minimize the problem.

   Also, the radioactivity adsorbed to the Teflon was assumed to be sulfluramid, but was not conclusively identified. It was stated that a variety of methods was used in an attempt to identify the absorbed radioactivity, but the presence of large amounts of fluors and emulsifiers in the scintillation solution made identification impossible. The study authors stated that, considering the location of the radiolabel on the sulfluramid molecule, any degradation of the molecule "would result in the release of a low molecular weight polar species...which would not selectively partition into a strongly hydrophobic Teflon matrix".

2. It was stated that detection limits were 0.001 ppm for the buffer solutions and 0.011 ppm for the toluene extracts, based on a counting volume of 500 uL for the buffers and 50 uL for the toluene extracts.

Sulfluramid

Page_____ is not included in this copy.

Pages 9 through 15 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

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_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

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DATA EVALUATION RECORD

SH#128992 STUDY 2 PM 18

CHEM Sulfluramid N-Ethylperfluorooctanesulfonamide 163-1
Company Code GX071 EPA PC #128992 (Unaged)

BRANCH: Environmental Fate and Ground Water

FORMULATION: Pure active ingredient, radiolabelled

Spare, W.C. 1991. Adsorption/Desorption of ^{14}C-GX071. Performed by Agrisearch, Inc. Frederick, MD. Laboratory Project No. 2515; Completed 1/16/92. Submitted by Griffin Corporation, Valdosta, GA.
MRID #42154701

REVIEWED BY: S.C. Termes
TITLE: Chemist
ORG: EAB/HED/OPP
TEL: (703) 305-5243

SIGNATURE: January 12, 1993

CONCLUSIONS

This study is acceptable and can be used towards partially fulfilling data requirements for the mobility of unaged GX071 in four different soils.

If the photodegradation in water and/or aerobic soil studies show that GX071 degrades a significant extent, studies (batch-equilibrium adsorption/desorption) with the major degradates may be required to address the "aged" portion of the mobility in soil (163-1) data requirement.

According to the results of the study, GX071 was immobile in four different soils, with Freundlich adsorption constants (K_{ads}) ranging from 118 to 2296 and K_{oc} values ranging from 22,383 to 267,130. The values of n ranged from 0.664 to 0.831, which is indicative that adsorption is non-linear. In spite of the attempts made to reduce adsorption to glassware/Teflon caps, adsorption onto the test system was significant but not surprising taking into consideration the chemical structure of the parent compound. Results are summarized below (for further information on the soils refer to Table A). The results also show that once adsorbed, GX071 doe not desorb back into the solution phase.

Series/Texture	Sharkey Clay	Sassafras Sand	Sequatchie Sandy Loam	Hesperia Loam
Source	Mississippi	Maryland	Maryland	California
n	0.783	0.831	0.664	0.667
K_{ads}	633	118	2296	1257
K_{oc}	22,436	22,383	205,466	267,130
%O.C. (%O.M.)	2.8 (4.8)	0.53 (0.9)	1.1 (1.9)	0.47 (0.8)
pH	5.9	6.5	7.5	6.7

MATERIALS AND METHODS

Test Substance: Analytical grade GX071 radiolabelled (C^{14}) at the C-1 position; specific activity 14.1 mCi/mM (New England Nuclear). Purified by performing laboratory to 99% (two single-dimension TLC solvent systems). Purity confirmed by GC. Solubility in water below 1 ppm at 25 C.

Soil: Studies were coducted in four different soils (a Sharkey clay from Mississippi, a Sassafras sand from Maryland, a Sequatchie sandy loam from Maryland, and a Hesperia loam from California). Soil characteristics are presented in Table 1. Soil origin and mineralogy were not provided. All soils were air dried and sieved (2 mm mesh) prior to use.

Test solutions: Filtered, deionized, boiled and distilled drinking water was used to prepare the "test solvent" (0.01 N in calcium ion; as calcium acetate). Because of the very low solubility of the test substabce in aqueous media, a stock solution of GX071 was prepared (12.4 mg/mL).

For the range finding study a test solution at a nominal concentration of 0.6 ug/mL was prepared by dilution of 0.01 mL of the stock solution in 200 mL test solvent. The test solutions for the definitive study were prepared by diluting 0.036 mL of the stock solution to 3 mL in methanol. From this solution, the test solutions in the test solvent were prepared at nominal concentrations of 0.3 ug/mL, 0.15 ug/mL, 0.075 ug/mL and 0.015 ug/mL. Studies with the test solvent alone were performed as control (i.e, 0.00 ug/mL concentration).

Test sytems: Test systems consisted of each capped centrifuge tube, with the soil (1 g for range finding study; 0.25 g for the definitive study); and the test solution(s). Mechanical shaking of the test systems was used; test systems were maintained at 23-25 C.

Experimental procedure: With the purpose of establishing a proper equilibration time, appropriate soil:solution ratio, and extent of adsorption to the container and caps, a preliminary range finding experiment was performed at 0.7 ug/mL of GX071. This study showed that equilibration was established rapidly; a 2-hr equilbration time was chosen (range finding study cover times of 2, 4, 8, 24, and 48 hrs). The appropriate soil:solution ratio was chosen as 0.25 g soil:25 mL of solution. Binding to the glass and Teflon caps caps was observed and attempts to reduce the binding of GX071 by silanizing (with methyltrimethoxysilane) or methylating (with diazomethane) the glassware and Teflon caps did not reduce the binding of GX071. For the definitive study the glassware and Teflon caps were not pretreated.

For the adsorption phase, test systems contained in 50 mL glass centrifuge tubes were studied in duplicate for each concentration (with blank samples at each concentration). After shaking (175- 200 rpm), the and centrifugation (15 min/1000 G) the equilibrium concentration of GX071 in solution (C_e) was determined by LSC. The actual concentration of GX071 adsorbed was determined by combustion of the soil (wet, after correction for residual solution). Methanol was added to each remaining sample set, reshaken for 15 min and the methanol phases quantified by LSC.

For the desorption phase, soils remaining from a definitive, separate adsorption test at concentrations of 0.07, 0.14, 0.18, 0.22, and 0.70 ug/mL (0.5 g soil and 50 mL solution) were weighed after removal of solution prior to adding 50 mL of the test solvent, followed by shaking for 4 hrs (175-200 rpm), centrifuged and the supernatant analyzed by LSC to determine C_e; soil concentration was determined by combustion and corrected as for the adsorption phase.

All samples were analyzed on the same day.

Calculations

The Freunlich equation was applied in the calculations,

$x/m = K_d C_e^{1/n}$ or $\ln(x/m) = \ln K_d + 1/n \ln C_e$

x/m= soil equilibrium concentration, ug/g
C_e equilibrium concentration in the aqueous phase, ug/mL
K_d= Freundlich adsorption constant
n= a constant

Values of $\ln C_e$ were plotted versus $\ln x/m$ for the adsorption and desorption phase; K_d and n were determined from intercept and slope (linear regression). The adsorption constant was also expressed in terms of soil organic carbon content,

$$K_{oc} = (K_d \times 100)/ \%O.C$$

O.C.= Organic carbon content, calculated as %O.C.= %O.M./1.7

Statistical methods for data reduction used were linear regression, means, sums and logarithms.

REPORTED RESULTS

The reported results indicate that GX071 adsorbed strongly onto the four soils, although there was competitive adsorption onto the glassware and Teflon caps, K_{ad} (Freundlich) constants ranging from 118 (sand) to 2296 (sandy loam) and $n < 1$. K_{des} were estimated assuming n= 1 since all desorption tests were

inappropriate for their evaluation; the estimated K_{des} ranged from 4445 (sand) and 11,320 (sandy loam).

K_{oc} values (adsorption) ranged from 22,383 (sand) to 267,130 (loam). All estimated K_{oc} values for the desorption phase were greater than 290,000.

The desorption phase stidy indicated that once GX071 had adsorbed onto the soil and/or glass, it adsorbed strongly and did not desorbed back into the solution phase.

REVIEWER'S COMMENTS

Although ideally adsorption onto test equipment is desired, attempts to prevent adsorption of the test material onto glassware/Teflon caps by two methods (silanization with methyltrimethoxysilane and methylation with diazomethane) were not effective. In spite of this, the results show clearly that the test substance adsorbs strongly onto soil as evidence by the high Freundlich adsorption constants ranging from 118 to 2296. The study also show that, once adsorbed to soils and/or test equipment, GX071 does not desorb back into the solution phase.

The strong tendency of GX071 to absorb onto soils and test equipment is likely related to the structural properties of the compound, which shows resemblance with many surface active agents. The values of n ranging from 0.664 to 0.831 indicates that the adsorption is non-linear. Non-linerity could arise from saturation of the binding sites and/or from competition for binding sites (for example, soil versus glassware/Teflon surfaces).

Sulfluramid

Page_____ is not included in this copy.

Pages 20 through 25 are not included.

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____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

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